IN THE CLAIMS

Claims 1-66 (canceled).

Claim 67 (currently amended): A method that is diagnostic or diagnostic and prognostic for precancer or cancer comprising contacting a mammalian sample with a **potent MN/**CA IX-specific inhibitor conjugated to a label or a visualizing means, and detecting or detecting and quantifying binding of said **potent MN/**CA IX-specific inhibitor to **MN/CA IX on** cells in said sample by detecting or detecting and quantifying said label or said visualizing means on cells in said sample, wherein said detection or said detection and quantitation at a level above that for a control sample is indicative of precancerous or cancerous cells that overexpress **MN/**CA IX in said sample**;**

wherein said inhibitor is selected from the group consisting of organic heterocyclic and aromatic compounds, and wherein said inhibitor is determined to be a potent inhibitor of MN/CA IX enzymatic activity in a screening assay comprising determining the inhibition constant K_I of said compound;

wherein if said inhibition constant K_I is determined to be less than about 50 nanomolar, said inhibitor is determined be a potent inhibitor of MN/CA IX enzymatic activity; and

wherein said potent inhibitor is determined to be an MN/CA IX-specific inhibitor if it is a more potent inhibitor of MN/CA IX enzymatic activity than of the enzymatic activity of each of the carbonic anhydrases in the group consisting of CA I, CA II and CA IV.

Claim 68 (currently amended): The method of claim 67 wherein **MN/**CA IX ~~activated by hypoxic conditions~~ is detected or detected and quantitated, and the mammal from whom the sample was taken is considered to have a poor prognosis, and decisions on treatment for said mammal are made in view of the ~~presence~~ **level** of said ~~hypoxic conditions~~ **MN/CA IX** .

Claim 69 (currently amended): A method for imaging tumors and/or metastases that express **MN/**CA IX in a patient comprising the administration of a **potent MN/**CA IX-specific inhibitor linked to an imaging agent to said patient;

wherein said inhibitor is selected from the group consisting of heterocyclic and aromatic organic compounds, and wherein said inhibitor is determined to be a potent inhibitor of MN/CA IX enzymatic activity in a screening assay comprising determining the inhibition constant K_I of said compound;

wherein if said inhibition constant K_I is determined to be less than about 50 nanomolar, said inhibitor is determined be a potent inhibitor of MN/CA IX enzymatic activity; and

wherein said potent inhibitor is determined to be an MN/CA IX-specific inhibitor if it is a more potent inhibitor of MN/CA IX enzymatic activity than of the enzymatic activity of each of the carbonic anhydrases in the group consisting of CA I, CA II and CA IV.

Claim 70 (currently amended): A diagnostic/prognostic method for a preneoplastic/neoplastic disease associated with abnormal MN/CA IX expression, comprising ~~determining whether~~ **detecting or detecting and quantifying** MN/CA IX ~~is activated~~ in a vertebrate sample, comprising:

a) contacting said sample with a **cell membrane-impermeant, potent** specific inhibitor of ~~activated~~ MN/CA IX, and

b) detecting or detecting and quantifying binding of said specific inhibitor of ~~activated~~ MN/CA IX in said sample;

~~wherein binding of said inhibitor to MN/CA IX indicates that MN/CA IX is activated~~

wherein said inhibitor is selected from the group consisting of cell membrane-impermeant heterocyclic and aromatic organic compounds, and wherein said inhibitor is determined to be a potent inhibitor of MN/CA IX enzymatic activity in a screening assay comprising determining the inhibition constant K_I of said inhibitor;

wherein if said inhibition constant K_I is determined to be less than about 50 nanomolar, said inhibitor is determined be a potent inhibitor of MN/CA IX enzymatic activity; and

wherein said potent inhibitor is determined to be an MN/CA IX-specific inhibitor if it is a more potent inhibitor of MN/CA IX enzymatic activity than of the enzymatic activity of CA IV.

Claim 71 (canceled).

Claim 72 (currently amended): The method of ~~claim 70~~ **claim 70** wherein said **cell membrane-impermeant MN/CA IX-**specific inhibitor ~~of activated MN/CA IX~~ is an MN/CA IX-specific **aromatic or heterocyclic** sulfonamide.

Claim 73 (currently amended): The method of claim 72 wherein said MN/CA IX-specific **aromatic or heterocyclic** sulfonamide is **a cell membrane-impermeant pyridinium derivative of** an aromatic or heterocyclic sulfonamide.

Claim 74 (currently amended): The method of claim 72 wherein said MN/CA IX-specific **aromatic or heterocyclic** sulfonamide is selected from the group consisting of Compounds 1-91.

Claim 75 (previously presented): The method of claim 72 wherein said MN/CA IX-specific sulfonamide is selected from the group consisting of Compounds 1-26 .

Claim 76 (currently amended): The method of claim [[71]] **70**, wherein said specific inhibitor of ~~activated~~ MN/CA IX is conjugated to a label or a visualizing means, wherein said detecting or detecting and quantifying binding comprises detecting or detecting and quantifying said label or said visualizing means on cells in said sample, and wherein said detecting or said detecting and quantifying at a level above that for a

control sample is indicative of ~~hypoxic~~ precancerous or cancerous cells that abnormally express ~~activated~~ MN/CA IX in said sample.

Claim 77 (previously presented): The method of claim 76, wherein said label is fluorescein isothiocyanate.

Claim 78 (previously presented): The method of claim 76, wherein said method is used as an aid in selection of patient therapy.

Claim 79 (currently amended): The method of claim 78, wherein said binding to ~~activated~~ MN/CA IX is detectable at a level above that for a control sample, and said method is used in the decision to use ~~hypoxia-selective~~ **MN/CA IX-targeted** therapy.

Claim 80 (currently amended): The method of claim [[79]] **78**, wherein said ~~hypoxia-selective~~ therapy comprises the use of ~~drugs that are toxic only under hypoxic conditions~~ **MN/CA IX-specific inhibitors, conventional anticancer drugs, chemotherapeutic agents, different inhibitors of cancer-related pathways, bioreductive drugs, radiotherapy, MN/CA IX-specific antibodies and MN/CA IX-specific antibody fragments that are biologically active**.

Claim 81 (currently amended): The method of claim [[80]] **76**, wherein said ~~hypoxia-selective therapy comprises the use of tirapazamine or AQ4N~~ **method is used to monitor the status of a cancer patient**.

Claim 82 (currently amended): The method of claim [[78]] **81**, wherein ~~said binding to activated MN/CA IX is not detectable at a level above that for a control sample, and~~ said method is used ~~in the decision to use radiotherapy or non-hypoxia-selective chemotherapy~~ **to monitor cancer chemotherapy and tumor reappearance, detect the presence of cancer metastasis, and/or confirm the absence or removal**

of all tumor tissue following surgery, cancer chemotherapy and/or radiation therapy.

Claim 83 (currently amended): A method of imaging ~~hypoxic tissues~~ **a tumor or tumors and/or metastases that express MN/CA IX** in a patient, comprising:

a) administering to said patient a **cell membrane-impermeant, potent** specific inhibitor of ~~activated~~ MN/CA IX, said inhibitor linked to an imaging agent; and

b) detecting the binding of said inhibitor**;**

wherein said inhibitor is selected from the group consisting of cell membrane-impermeant heterocyclic and aromatic sulfonamides, and wherein said inhibitor is determined to be a potent inhibitor of MN/CA IX enzymatic activity in a screening assay comprising determining the inhibition constant K_I of said inhibitor, wherein if said inhibition constant K_I is determined to be less than about 50 nanomolar, said inhibitor is determined be a potent inhibitor of MN/CA IX enzymatic activity; and

wherein said potent inhibitor is determined to be an MN/CA IX-specific inhibitor if it is a more potent inhibitor of MN/CA IX enzymatic activity than of the enzymatic activity of CA IV.

Claim 84 (currently amended): The method of claim 83 wherein said specific inhibitor of ~~activated~~ MN/CA IX is ~~an MN/CA IX-specific~~ **a positively-charged, membrane-impermeant aromatic or heterocyclic** sulfonamide.

Claim 85 (new): The method of claim 84 wherein said membrane-impermeant sulfonamide is a pyridinium derivative of an aromatic or heterocyclic sulfonamide.

Claim 86 (new): The method of claim 72 wherein said MN/CA IX-specific sulfonamide is selected from the group consisting of Compounds 27-70.

Claim 87 (new): The method of claim 67 wherein said group consisting of organic heterocyclic and aromatic compounds is a group consisting of heterocyclic and aromatic sulfonamides.

Claim 88 (new): The method of claim 87 wherein said group consists of Compounds 1-91.

Claim 89 (new): The method of claim 69 wherein said group consisting of organic heterocyclic and aromatic compounds is a group consisting of heterocyclic and aromatic sulfonamides.

Claim 90 (new): The method of claim 89 wherein said group consists of Compounds 1-91.